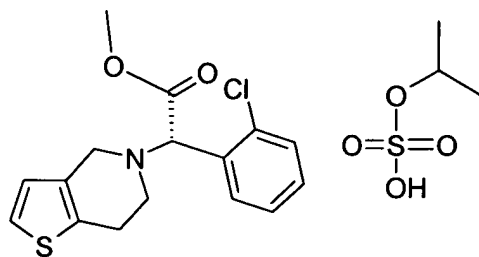


## APPENDIX B

**Process for the preparation of a salt of clopidogrel with isopropyl-sulphate**

In a boiling mixture of 22 ml of acetone and 20 ml of 2-propanol 3,0 g of clopidogrel hydrogensulphate of polymorph form 1 is dissolved. The mixture is slowly cooled to room temperature then kept in fridge overnight. The precipitated crystals filtered and washed with cold acetone.

Yield: 2.18 g (66%)

Analysis:  $C_{19}H_{24}ClNO_6S_2$  (461.99)

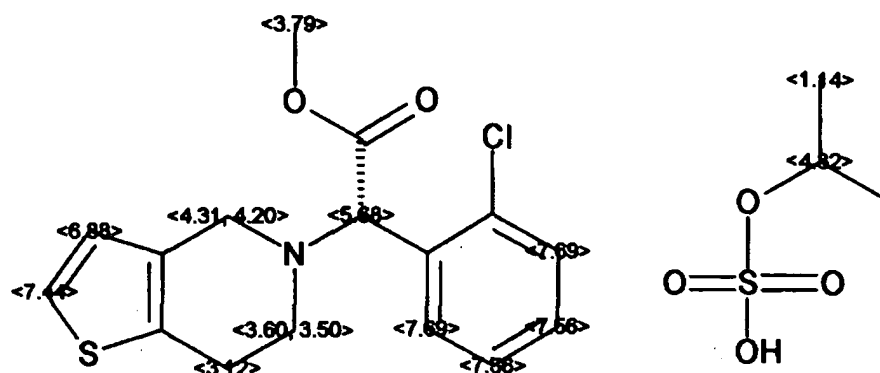
Calculated: C 49.40 %; H 5.24 %; Cl 7.67 %, N 3.03 %, S 13.88 %

Found: C 49.30 %; H 5.31 %; Cl 7.82 %; N 3.19 %, S 14.01 %.

IR,  $^1H$ -NMR and  $^{13}C$ -NMR, X-ray diffractogram are enclosed

Leadási dátum:	2001.10.09.	mérések:	IR, HNMR, CNMR	Jegyzőkönyv:	IGEN
J.k. dátuma:	2001.10.11.	Mérések:	IR, HNMR, CNMR		

<sup>1</sup>H hozzárendelések:



DMSO-D<sub>2</sub>

<sup>13</sup>C (v. X) hozzárendelések:

IR (KBr): 3442, 1755, 1284, 1037.

<sup>1</sup>H NMR (DMSO-D<sub>2</sub>O, 400): 7.69 (m, 2H), 7.56 (m, 2H), 7.44 (d, J=5.2 Hz, 1H), 6.88 (d, J=5.1 Hz, 1H), 5.68 (s, 1H), 4.32 (bp, J=6.2 Hz, 1H), 4.31 (d, 1H), 4.20 (d, J=14.7 Hz, 1H), 3.79 (s), 3.60 (m, 1H), 3.50 (m, 1H), 3.12 (m, 2H), 1.14 (d, J=6.3 Hz, 6H).

<sup>13</sup>C NMR: 167.93, 134.94, 133.03, 132.21, 131.30, 130.71, 129.15, 128.67, 128.21, 125.99, 125.80, 69.98, 66.07, 54.39, 50.93, 49.78, 23.56, 22.78.

Jegyzőkönyv:

A spektrumok megfelelnek a feltételezett szerkezetnek. IPA hozzáadással bizonyítottuk, hogy a spektrumban látható 1 mol iPrO- csoport nem izopropanoltól származik.

## STANDARD 1H OBSERVE

40660  
S2583  
Kotay Nagy, Peter  
01/10/10(NM)

Solvent: DMSO  
Temp. 25.0 C / 298.1 K  
File: 406601h  
INVA-500 "1500"

## PULSE SEQUENCE

Relax. delay 5.000 sec  
Pulse 39.1 degrees  
Acq. time 3.003 sec  
Width 6000.2 Hz  
16 repetitions

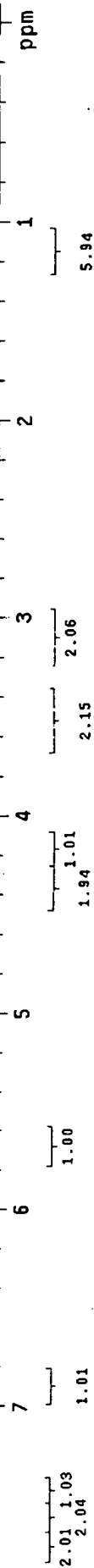
OBSERVE H1 400.0087959 MHZ

## DATA PROCESSING

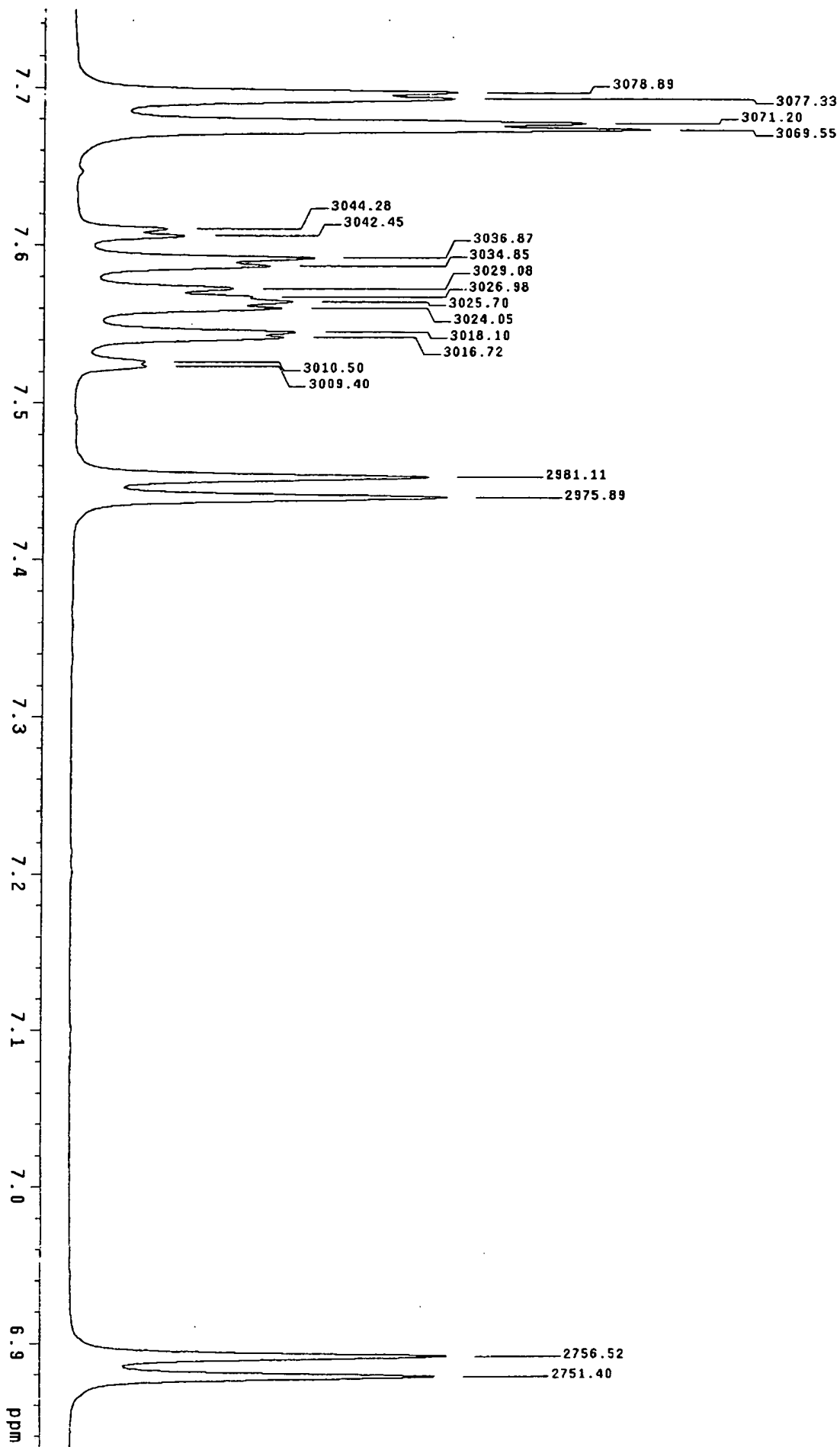
FT size 131072  
Total time 2 minutes

FREQUENCY	PPM	HEIGHT
1014.873	2.537	47.7
1013.133	2.533	65.3
1011.393	2.528	49.0
460.598	1.151	348.7
454.281	1.136	345.7
0.077	0.000	8.7

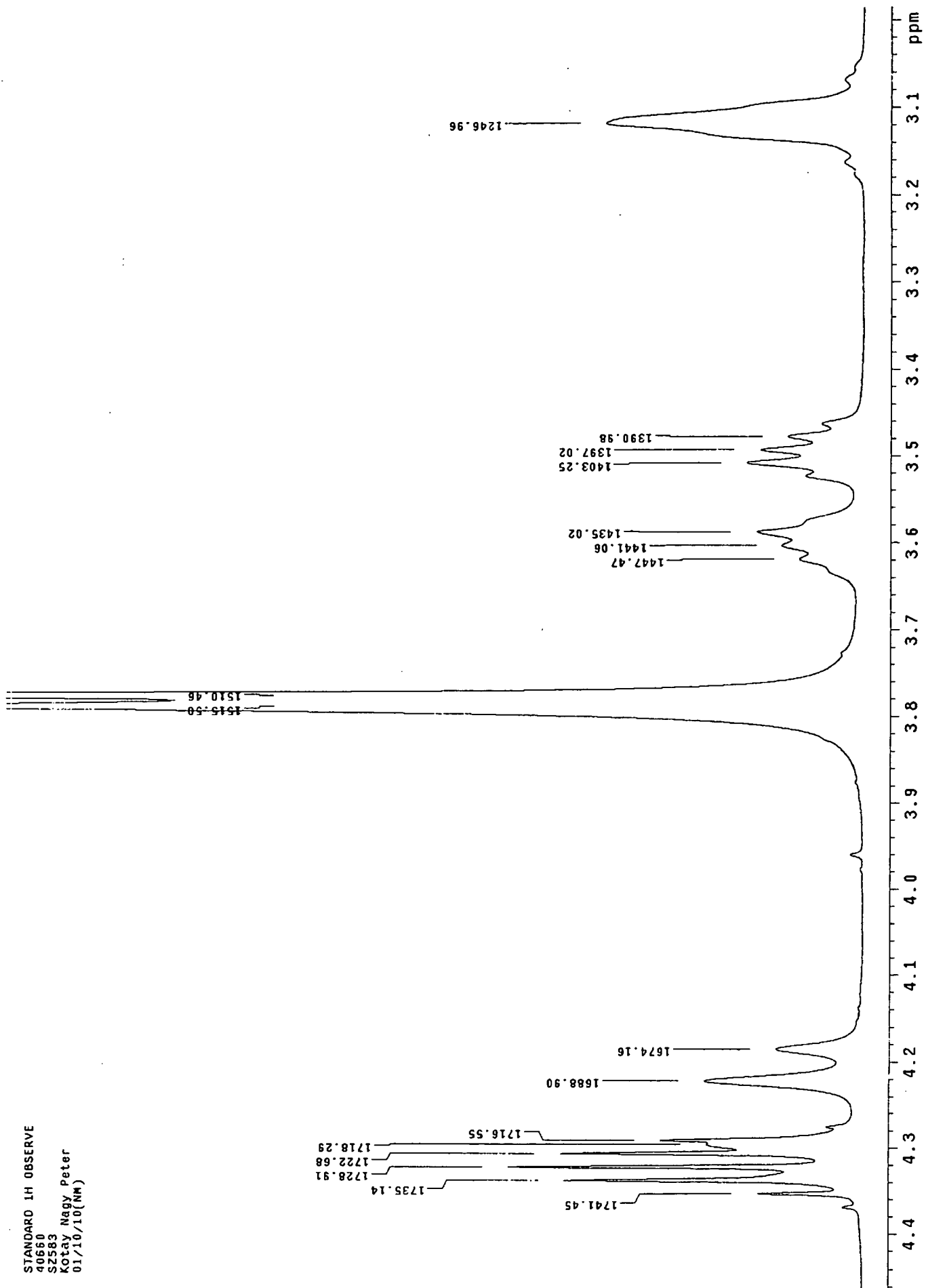
INDEX	FREQUENCY	PPM	HEIGHT	INDEX
1	3078.889	7.697	45.0	40
2	3077.333	7.693	44.7	41
3	3071.198	7.678	60.1	42
4	3069.550	7.674	67.6	43
5	3044.281	7.611	11.2	44
6	3042.450	7.606	13.2	45
7	3036.865	7.592	28.2	
8	3034.851	7.587	23.1	
9	3029.083	7.573	18.8	
10	3026.977	7.567	21.0	
11	3025.696	7.564	25.7	
12	3024.048	7.560	24.4	
13	3018.096	7.545	26.0	
14	3016.723	7.542	24.7	
15	3010.497	7.526	8.5	
16	3009.399	7.523	8.7	
17	2981.108	7.453	41.8	
18	2975.890	7.440	44.0	
19	2756.524	6.891	44.2	
20	2751.397	6.878	42.8	
21	2270.550	5.676	69.8	
22	1741.453	4.354	11.1	
23	1735.136	4.338	31.7	
24	1728.910	4.322	37.7	
25	1722.684	4.307	32.1	
26	1718.290	4.296	16.5	
27	1716.550	4.291	21.5	
28	1688.901	4.222	16.8	
29	1674.160	4.185	9.2	
30	1515.495	3.789	103.6	
31	1510.460	3.776	291.9	
32	1447.470	3.619	6.9	
33	1441.061	3.603	8.8	
34	1435.019	3.587	11.5	
35	1409.292	3.523	6.3	
36	1403.249	3.508	12.6	
37	1397.023	3.492	11.1	
38	1390.981	3.477	8.2	
39	1246.965	3.117	27.6	



STANDARD 1H OBSERVE  
40660  
S2583  
Kotay Nagy Peter  
01/10/10(NM)



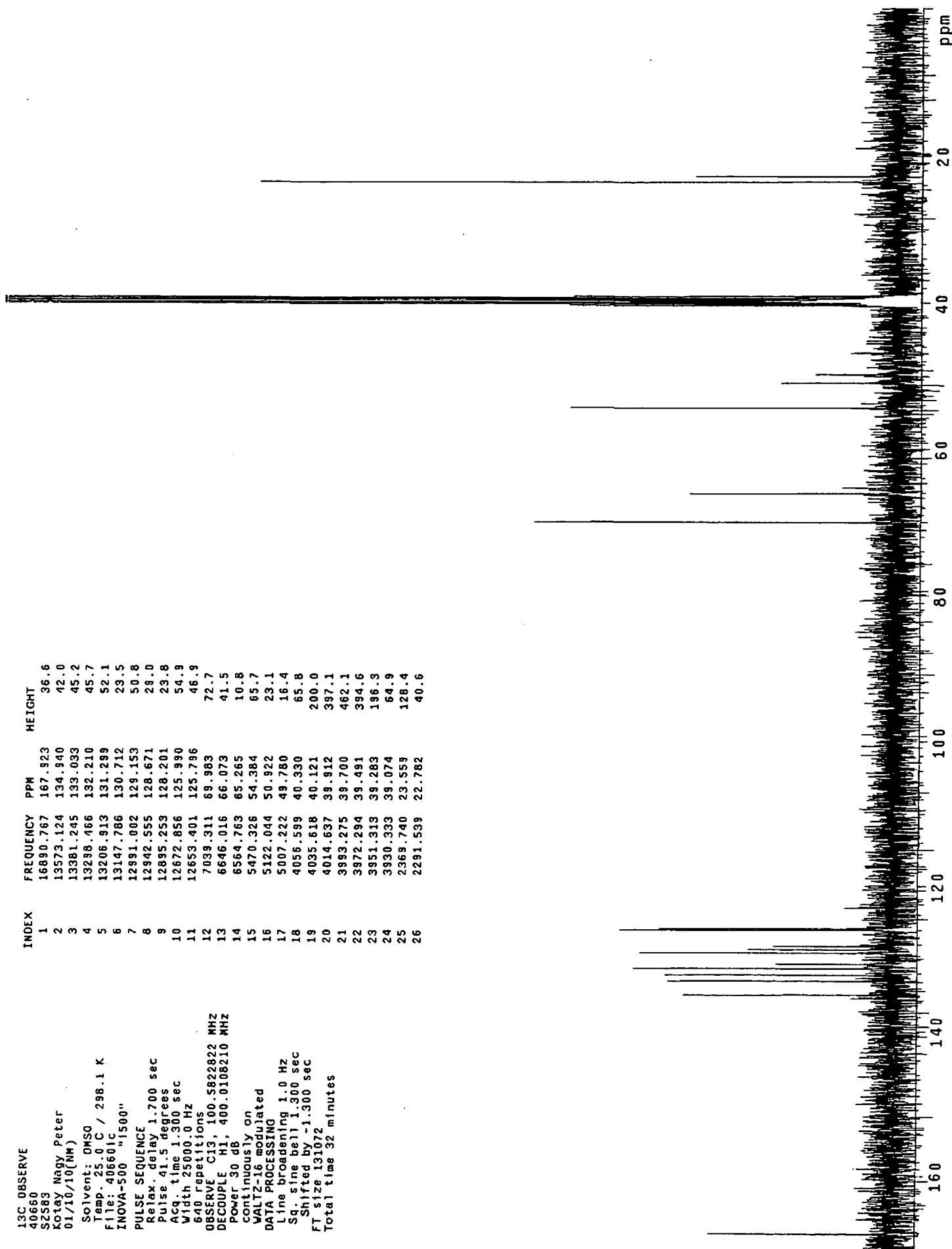
STANDARD 1H OBSERVE  
40660  
SZ583  
Kotay Nagy Peter  
01/10/10(NM)



**13C OBSERVE**

40660  
S2583  
Kotay Nagy Peter  
01/10/10(MW)  
Solvent: DMSO  
Temp: 25.0 C / 298.1 K  
File: 406601C  
INOVA-500 "1500"  
PULSE SEQUENCE  
Relax. delay 1.700 sec  
Pulse 41.5 degrees  
Acq. time 1.300 sec  
Width 25000.0 Hz  
640 repetitions  
OBSERVE C13, 100.5822822 MHz  
DECOUPLE H1, 400.0108210 MHz  
Power 30 dB  
continuously on  
WALTZ-16 modulated  
DATA PROCESSING  
Line broadening 1.0 Hz  
Sq. sine bell 1.300 sec  
Shifted by -1.300 sec  
FT size 131072  
Total time 32 minutes

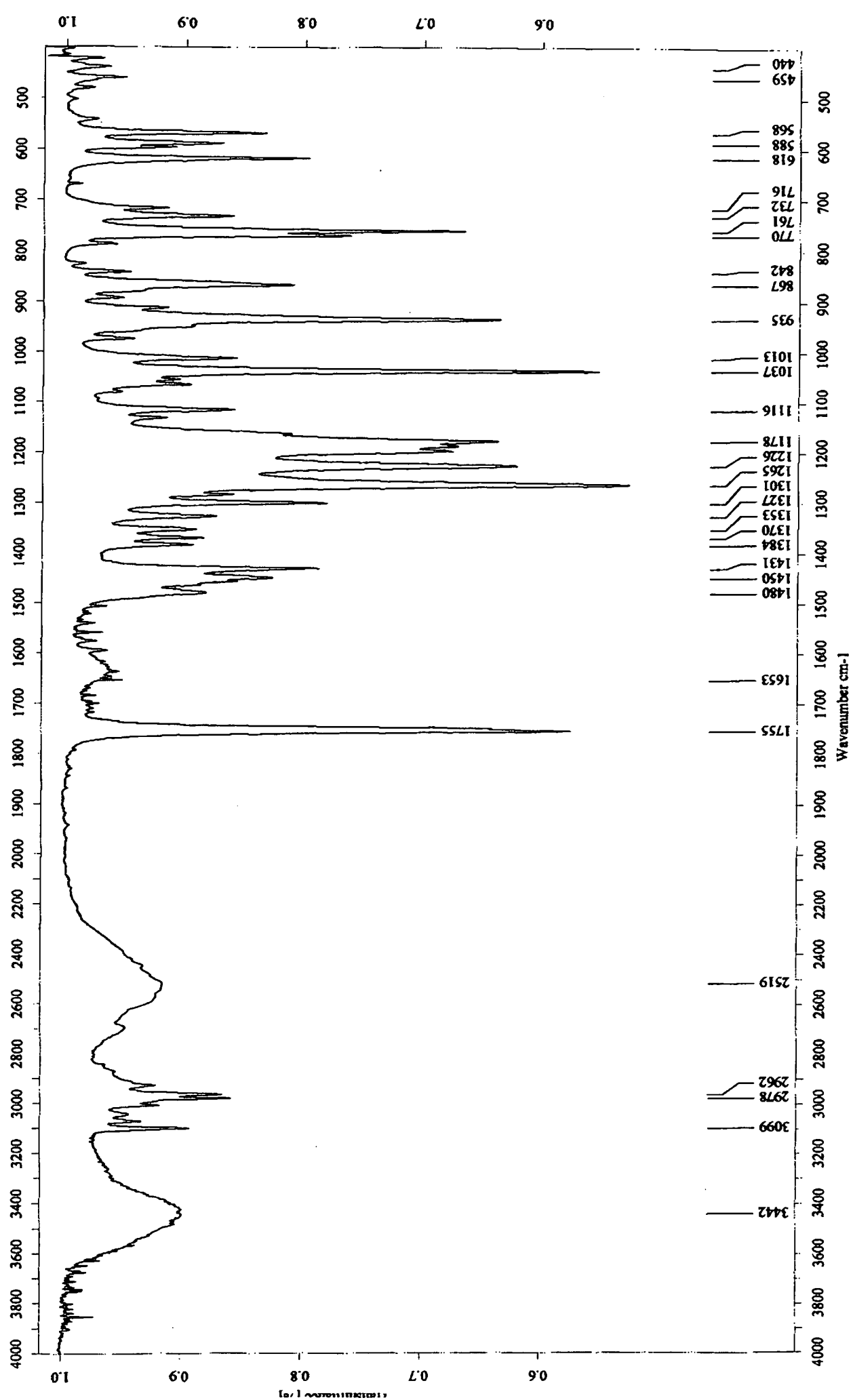
INDEX	FREQUENCY	PPM	HEIGHT
1	16890.767	167.923	36.6
2	13573.124	134.940	42.0
3	13381.245	133.033	45.2
4	13298.466	132.210	45.7
5	13206.913	131.289	52.1
6	13147.786	130.712	23.5
7	12991.002	129.153	50.8
8	12942.555	128.671	28.0
9	12895.253	128.201	23.8
10	12872.856	125.990	54.9
11	12653.401	125.796	46.9
12	7039.311	69.983	72.7
13	6646.016	66.073	41.5
14	6564.763	65.265	10.8
15	5470.326	54.384	65.7
16	5122.044	50.922	23.1
17	5007.222	49.780	16.4
18	4056.599	40.330	65.8
19	4035.618	40.121	200.0
20	4014.637	39.812	397.1
21	3983.275	39.700	462.1
22	3872.294	39.491	394.6
23	3951.313	39.283	186.3
24	3830.333	39.074	64.9
25	2369.740	23.559	128.4
26	2291.539	22.782	40.6



**0660**  
**Z583**

Kótyay-Nagy Péter  
KBr

BRUKER VECTOR22  
Resolution: 2 cm-1  
Number of Scans: 8



CLOP18 Clopidogrel KF-69/16 04-04-2001 1.54186 Cu 40 30 0.04 4.5-34.9 1421  
 CLOP22 Clopidogrel 1612 sz583 05-09-2001 1.54186 Cu 40 30 0.04 4.5-34.9 1962

